

II. Remarks

Claims 1, 2, 4, 5, 7-12 and 39-52 are pending. Certain amendments have been made to the present claims to clarify the specific order of steps, as well as the application of the method to particular active agents. Support for these amendments is provided, *inter alia*, at pages 34, line 14 through page 35, line 11. No new matter has been added by these amendments. Reconsideration of this application, in view of the amendments to the claims and the arguments presented herein, is respectfully requested.

The examiner's acknowledgement of the submissions of the Information Disclosure Statement disclosing the reference relating to the high-shear mixer, and the amendment to the specification to include cross-reference to the related applications is appreciated.

Still, certain rejections have been maintained and are addressed below.

A. Obviousness-type Double Patenting Rejection

In the instant Office Action, a nonstatutory obviousness-type double patenting rejection has been maintained for claims 1, 2, 4-5, 7-12 and 51-52 as being unpatentable over claims 20, 21 and 23-27, and for claims 39-42 and 46-50 as being unpatentable over claims 25-27 of U.S. Patent No. 6,103,219. An obviousness-type double patenting rejection has also been maintained against claims 39-42 and 46-50 as being unpatentable over claims 19, 20, 24, 30, 32 and 33 of U.S. Patent No. 6,746,693. A Terminal Disclaimer citing both U.S. Patent Nos. 6,103,219 and 6,746,693 is submitted herewith. Applicants believe this submission of the Terminal Disclaimer obviates all outstanding obviousness-type double-patenting rejections, and respectfully request withdrawal of these rejections.

B. 35 U.S.C. §103 Rejections

In the Office Action, the Examiner also rejected claims 1, 2, 4, 5, 7-12 and 39-52 under 35 U.S.C. §103(a) as being unpatentable over United States Patent No. 4,605,666 to Schmidt et al.

("Schmidt"). The Examiner stated that "Schmidt teaches a 'process for preparing a powder ... which is directly compressible into a tablet prepared by spray drying (a) an aqueous slurry of water soluble vitamin and a binder; (b) ... an adsorbent; and (c) a lubricant' (Abstract)." The Examiner also stated "[i]t is taught that the powders are directly compressible into tablets ..." The Examiner further stated that "[i]n example 1 an aqueous slurry of ascorbic acid, microcrystalline cellulose and water is spray dried and silicon dioxide is added (Col. 3, lines 29-49) ... [and that] [t]he adsorbent is silicon dioxide (Col. 7, lines 14-15) and the binder is microcrystalline cellulose (Col. 8, lines 4-5)."

The Examiner then concluded that "a person having ordinary skill in the art at the time the invention was made could have used the aqueous slurry taught by Schmidt and included the adsorbent silicon dioxide into the slurry prior to spray drying instead of adding it to the spray dried mixture. This would have been part of the routine experimentation strategy to optimize the compressibility of the final tablet." The Examiner also stated that "[p]rior to tableting, the excipients and active ingredient are mixed; therefore a 'plurality of agglomerated particles' would be achieved."

The Examiner also concluded that "[r]egarding instant claim 39, a person having ordinary skill in the art could use the teaching of Schmidt and prepare separate aqueous slurries of microcrystalline cellulose and silicon dioxide prior to spray drying as part of routine experimentation in order to determine which resultant excipient offered the best compressibility."

The Examiner's rejection is respectfully traversed. Independent claim 1 of the present invention now recites, in pertinent part, a method for preparing a tablet comprising... "forming an aqueous slurry containing a mixture of microcrystalline cellulose in the form of a wet cake and silicon dioxide ... ; drying said slurry to obtain an excipient comprising a plurality of agglomerated particles of microcrystalline cellulose in intimate association with said silicon dioxide ... [and] *then* mixing a moisture-sensitive active agent with said excipient ..."

Independent claim 39 of the present invention (also as amended herein) recites, in pertinent part, "(a) forming an aqueous slurry of microcrystalline cellulose in the form of wet cake; (b) forming an aqueous slurry of silicon dioxide having a particle size of from about 1 nm to about 100

µm; (c) separately introducing said microcrystalline cellulose slurry and said silicon dioxide slurry separately into a drying apparatus for combination therein, to obtain an excipient comprising a plurality of agglomerated particles of microcrystalline cellulose in intimate association with said silicon dioxide ... [and] (d) mixing a moistures-sensitive active ingredient with said excipient ...”. Thus, the subject invention is directed to first making the excipient and then adding a specific class of active ingredient to that excipient.

By contrast, the Schmidt reference describes a process for preparing an aqueous slurry which contains active ingredient, i.e., the excipient is not made prior to adding of the active, as in the case of the subject invention. Specifically, the cited reference of Schmidt describes a method where the active ingredient is added into the aqueous slurry. Accordingly, the process of Schmidt does not describe a method which can be used with a moisture-sensitive active ingredient as claimed for the subject method.

A moisture-sensitive active ingredient added with the aqueous slurry according to the method of Schmidt can result in detrimental effects on a moisture-sensitive active. The subject invention advantageously avoids such detrimental effects on a moisture-sensitive active agent by first making the excipient, then drying the excipient to provide a low moisture-containing excipient prior to addition of the moisture-sensitive active agent.

There is no teaching or suggestion provided by Schmidt that the water-soluble vitamin could be added after formation of the excipient, as claimed, because the aqueous slurry of Schmidt, which includes the water-soluble vitamin as active agent, dissolves the vitamin and thereby incorporates the active in its dissolved form into the compressible mixture. The water-soluble vitamin of Schmidt would be provided as an aqueous solution whether added to the slurry, or added after the slurry was formed and dried as a separate excipient. Thus, the Schmidt reference fails to provide a basis for a person having ordinary skill in the art at the time of the invention to form a “pre-manufactured” excipient comprising a plurality of agglomerated particles of microcrystalline cellulose in intimate association with the silicon dioxide, prior to the addition of a moisture-sensitive active agent, which

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advantageously protects the moisture-sensitive active, as provided by the subject invention.

The method of Schmidt, using a water soluble active, would not have led a person of ordinary skill in the art to the invention as claimed because the active would have been added into the aqueous slurry or as an aqueous solution prior to drying and compression.. Accordingly, it is respectfully submitted that independent claim 1 and the claims that depend therefrom, and independent claim 39 and the claims that depend therefrom, would not have been obvious under 35 U.S.C. § 103(a) in view of the Schmidt reference. Therefore, Applicants respectfully request that the Examiner's rejection be removed upon reconsideration.

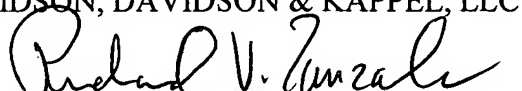
IV. Conclusion

This Amendment is being submitted together with a Request for Continued Examination and a Petition for a one (1) month extension of time under 37 C.F.R. § 1.136(a) along with a check in the amount of \$1190.00, to cover the \$810.00 Request for Continued Examination fee, and \$120 Petition for a one (1) month extension of time under 37 C.F.R. § 1.136(a) fee.

In view of the amendments made and arguments presented, it is respectfully submitted that the present application is now in condition for allowance. An early and favorable action on the merits is earnestly solicited. According to currently recommended Patent Office policy, the Examiner is specifically authorized to contact the undersigned in the event that a telephonic interview will advance the prosecution of the application.

Respectfully submitted,
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